

# Ultrasonography and Doppler Study to Predict Uterine Receptivity in Infertile Patients Undergoing Embryo Transfer and its Correlation with Pregnancy Rate

Anshikha Arora<sup>1</sup>, Jai K Goel<sup>2</sup>, Ruchica Goel<sup>3</sup>, Shashi B Arya<sup>4</sup>, Neeraj Prajapati<sup>5</sup>

## ABSTRACT

**Aim:** To study ultrasonographic and Doppler parameters to predict uterine receptivity in infertile patients undergoing embryo transfer (ET) and its correlation with pregnancy.

**Materials and methods:** It was a prospective interventional study, conducted in the *in vitro* fertilization unit of the Department of Obstetrics and Gynecology at Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, on 60 patients who presented with infertility. Transvaginal ultrasound was done on the day of adding progesterone in the frozen ET cycle and the day of trigger in the stimulation cycle. To assess uterine receptivity, we analyzed the ultrasonographic and Doppler parameters. The original Applebaum uterine scoring system was used. This uterine scoring system included ultrasound parameters: endometrial thickness, endometrial layering, and myometrial echogenicity and Doppler parameters: endometrial blood flow, uterine artery pulsatility index (PI), myometrial contractions, and myometrial blood flow. Ovum pickup was done 36 hours after the trigger. Day 3 or day 5 good quality embryos were transferred. Serum beta-human chorionic gonadotropin was performed 14 days after ET to confirm the pregnancy.

**Results:** Out of the 60 infertile patients who underwent ET, 38.3% conceived. Patients with a total score of 17–19 had a higher pregnancy rate of 62%. PI, myometrial contraction, and total Applebaum uterine score parameters were significantly ( $p < 0.05$ ) higher among patients with pregnancy than without pregnancy.

**Conclusion:** Transvaginal sonography and color Doppler for predicting uterine receptivity by means of Applebaum uterine scoring system are simple, quick, effective, and reproducible methods.

**Clinical significance:** Uterine scoring helps us in deciding whether ET should be performed in the present cycle or not.

**Keywords:** Assisted reproductive technique, *In vitro* fertilization, Pulsatility index.

*Journal of South Asian Federation of Obstetrics and Gynaecology* (2021); 10.5005/jp-journals-10006-1897

## INTRODUCTION

Infertility is defined as failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. According to the World Health Organization, the overall prevalence of primary infertility in India is between 3.9% and 16.8%. Due to changes in social behavior i.e. late marriages, job priorities, and unexplained infertility, the focus of treatment has deviated from systematic correction of each identified factor to providing the most efficient and cost-effective treatment, which is assisted reproductive technology (ART).

ART has given a new ray of hope for infertile couples. ART procedures include *in vitro* fertilization (IVF), embryo transfer (ET), gamete intrafallopian transfer, and zygote intrafallopian transfer. The oldest technique of all is IVF whereby the egg and sperm are brought in close proximity to facilitate fertilization.

The embryo and the endometrium are the important factors governing the outcome of an IVF cycle. Cross-talk between embryo and endometrium is important for a successful pregnancy. Endometrial receptivity is defined as a sequence of factors that make the endometrium receptive to embryonic implantation. There is no 100% successful method to predict uterine receptivity. Various methods for predicting uterine receptivity include biochemical markers, histological markers, endometrial receptivity array, and ultrasonographic scoring systems.<sup>1</sup> High-resolution transvaginal ultrasonography is considered a good noninvasive method for the assessment of endometrial receptivity.

<sup>1-4</sup>Department of Obstetrics and Gynaecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India

<sup>5</sup>Department of Radiodiagnosis, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India

**Corresponding Author:** Anshikha Arora, Department of Obstetrics and Gynaecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India, Phone: +91 07599900459, e-mail: anshikaarorambbs@gmail.com

**How to cite this article:** Arora A, Goel JK, Goel R, *et al.* Ultrasonography and Doppler Study to Predict Uterine Receptivity in Infertile Patients Undergoing Embryo Transfer and its Correlation with Pregnancy Rate. *J South Asian Feder Obst Gynae* 2021;13(3):146–150.

**Source of support:** Nil

**Conflict of interest:** None

The concept of evaluating uterine receptivity by means of a uterine scoring system for reproduction (USSR) or uterine biophysical profile was developed by Applebaum in 1995. For obtaining optimum results in favorable uteri, it has become an absolute necessity to evaluate the uterus and endometrium prior to ET.

Therefore, this study aims to evaluate uterine receptivity by using the Applebaum scoring system and study the relationship of ET with pregnancy in a North Indian tertiary care center.

**MATERIALS AND METHODS**

This study was conducted in the IVF unit of the Department of Obstetrics and Gynecology in collaboration with the Department of Radiodiagnosis at Shri Ram Murti Smarak Institute of Medical Sciences, Bhojipura, Bareilly. This study was conducted between November 2018 and May 2020 on a total of 60 patients attending infertility clinic with 20–45 years of age and duration of infertility ranging from 2–20 years. Patients with uterine anomalies and endometrial pathology were excluded from the study. The study protocol was explained to the patient in detail and informed written consent was obtained from them.

All patients in the fresh cycle were given antagonist protocol. They were stimulated with Recombinant Follicle Stimulating Hormone + Human Menopausal Gonadotropin (rFSH + HMG). Antagonist cetrorelix 0.25 µg was added using a flexible regimen till the day of trigger, and the trigger was done when three or more follicles of size 18 mm were seen. Transvaginal sonography (TVS) was done on the day of trigger. Either Inj leuprolide 1 mg s/c or HCG 10,000 IU I/M was given. In patients with frozen cycle, on day 1 estradiol valerate 2 mg TDS was started and TVS was done on the day of adding progesterone. All the patients who were not stimulated were taken as the frozen cycle for predicting endometrial receptivity. TVS was done by the same radiologist using Siemens ultrasound machine, Acuson with 4–9 MHz transvaginal probe, and scoring was done by Applebaum score as shown in Table 1.

Endometrial thickness was measured in millimeters as the maximal distance between the myometrial–endometrial junction and the endometrial–myometrial junction in a longitudinal plane of the uterus.

Endometrial layering—In the longitudinal plane—The endometrial pattern was visualized as having no layering, hazy five-line appearance, or distinct five-line appearance.

Myometrial echogenicity—The myometrium was studied on a longitudinal scan of the uterus and categorized as coarse/inhomogeneous echogenicity or completely homogeneous echogenicity.

The presence or absence of blood flow in zone 3 of the endometrium, which was the hypoechoic inner layer, was noted.

Uterine artery Doppler flow evaluation—Pulsatility index (PI) of both the right and left uterine artery was measured at the level of the cervix by using 2D color Doppler. The average of both was taken into consideration.

Myometrial blood flow—It was measured internal to the arcuate vessel. The presence, absence, or reversal of end-diastolic blood flow was recorded.

Myometrial contraction was seen as endometrial motion. Myometrial contractions propagate from the internal cervical os toward the uterine fundus in the late follicular phase.

Ovum pickup was done 36 hours after the trigger under ultrasound guidance. Day 3 or day 5 good quality embryos were transferred under ultrasound guidance. Serum beta-human chorionic gonadotropin was performed 14 days after ET to confirm the pregnancy.

**Statistical Analysis**

The results are presented in frequencies, percentages, and mean ± SD. The Chi-square and Fisher’s exact tests were used to compare categorical variables between the groups. The unpaired *t*-test was used to compare continuous variables between the groups at different time periods. The *p*-value <0.05 was considered

**Table 1:** Applebaum uterine scoring system

<i>Parameters</i>	<i>Score</i>
<b>Endometrial thickness</b>	
<7 mm	0
7–9 mm	2
10–14 mm	3
>14 mm	1
<b>Endometrial layering</b>	
No layering	0
Hazy five-line appearance	1
Distinct five-line appearance	3
<b>Endometrial blood flow within zone 3</b>	
Absent	0
Present, but sparse	2
Present multifocal	5
<b>Myometrial echogenicity</b>	
Coarse/inhomogeneous echogenicity	1
Relatively homogeneous echogenicity	2
<b>Uterine artery Doppler flow evaluated by PI</b>	
PI >3.0	0
PI ≥2.5–2.99	0
PI ≥2.2–2.49	1
PI <2.19	2
<b>Myometrial blood flow</b>	
Absent	0
Present	2
<b>Myometrial contractions</b>	
<3 contractions in 2 minutes (real-time)	0
>3 contractions in 2 minutes (real-time)	3
Total	20

significant. The receiver-operating characteristic (ROC) curve analysis was performed to determine the best predictive value. All the analysis was carried out on a Statistical Package for Social Sciences (SPSS) 16.0 version (Chicago, Inc., USA).

**RESULTS**

In our study, the mean age of patients was 33.33 ± 5.22 years with a maximum number of patients having normal BMI i.e. 78.3%, out of which 40.2% conceived.

Out of the total, 77% of the couples had primary infertility of which 35% conceived and 23% had secondary infertility, out of which 50% conceived. Thirty-five percentage of patients had 4–6 years of infertility, out of which 42% conceived.

The frozen cycle was done in 60% of the patients and the remaining 40% of patients underwent a fresh cycle. Maximum patients conceived in the frozen cycle.

The poor ovarian reserve was the most common cause of infertility i.e. in 45% of the patients. The tubal factor was the second most common cause of infertility i.e. 18.3%.

The total number of patients included in this study was 60, out of which 23 conceived with a pregnancy rate of 38%.

As shown in Figure 1, endometrial thickness of >7 to ≤9 mm was seen among 37 patients, out of which 14 conceived with a pregnancy rate of 37.8%. The highest pregnancy rate of 47.1% was seen with thickness >9 to ≤14 mm. No pregnancy was observed with endometrial thickness >14 mm.

Distinct five-line endometrium was seen in 53 patients, out of which 20 conceived with a pregnancy rate of 37.7%. Five patients had hazy five-line appearance, out of which two conceived. Two patients had no layering, out of which one conceived.

Relatively homogeneous echogenicity was present in 53 patients, out of which 20 conceived with a pregnancy rate of 37.7%. Coarse echogenicity was seen in seven patients, out of which three conceived.

Myometrial contractions were equally distributed in both the groups with conception rate maximum i.e. 56.7% in patients among whom myometrial contractions were >3 contractions in 2 minutes.

Figure 2 shows that multifocal endometrial vascularity in zone 3 was associated with 42% conception. Sparse blood flow was present

in five patients of which none conceived. Out of the five patients with absent endometrial blood flow, two conceived.

Maximum patients i.e. 23 had PI between 2.2 and 2.49 with a conception rate of 47.8%. PI values of ≥2.5 had a success rate of only 12%. PI of more than 3 was present in three patients with no pregnancy. PI <2.19 was favorable for pregnancy giving a success rate of 50%. There was a statistically significant ( $p = 0.02$ ) association of pregnancy rate with PI. Myometrial blood flow was observed in all patients.

Figure 3 shows that out of 24 patients who had a score between 17 and 19, 15 conceived giving a pregnancy rate of 62.5%. Twenty-five patients had scores of 14–16 of which 6 conceived giving a pregnancy rate of 24% and 10 patients with score <13 of which 2 conceived.

The total score >15 was calculated by ROC curve as shown in Figure 4, correctly predicted pregnancies in 33.3% of the total 38.3% patients with sensitivity and specificity of 87% and 59.5%, respectively. The positive predictive value was 57.1%, and the negative predictive value was 88%. The area under the curve was 0.74, which was fairly significant.

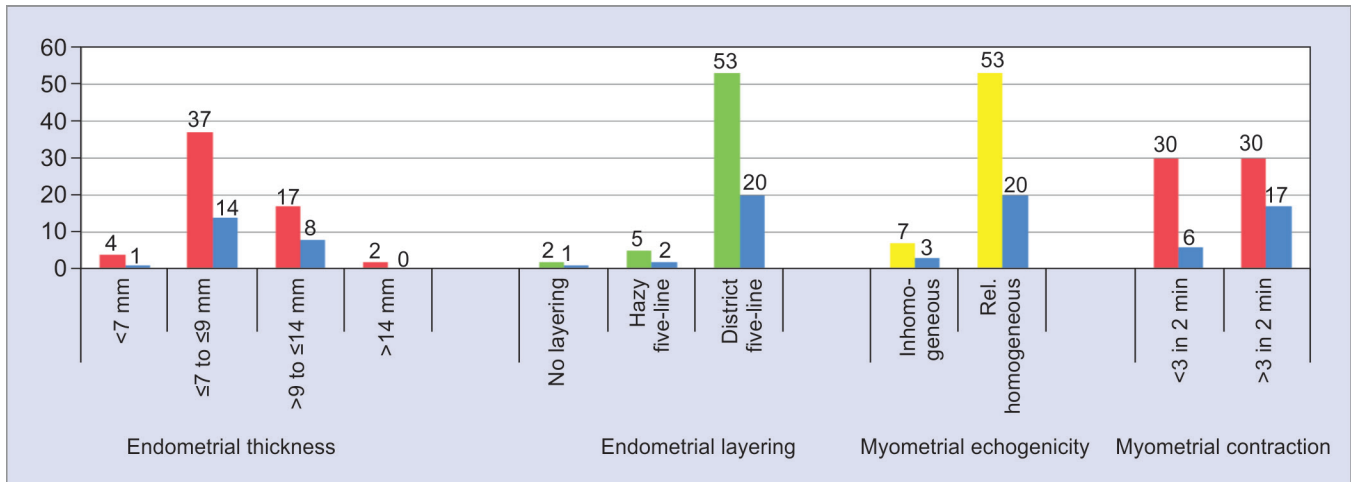


Fig. 1: Correlation of ultrasonographic parameters with pregnancy rate

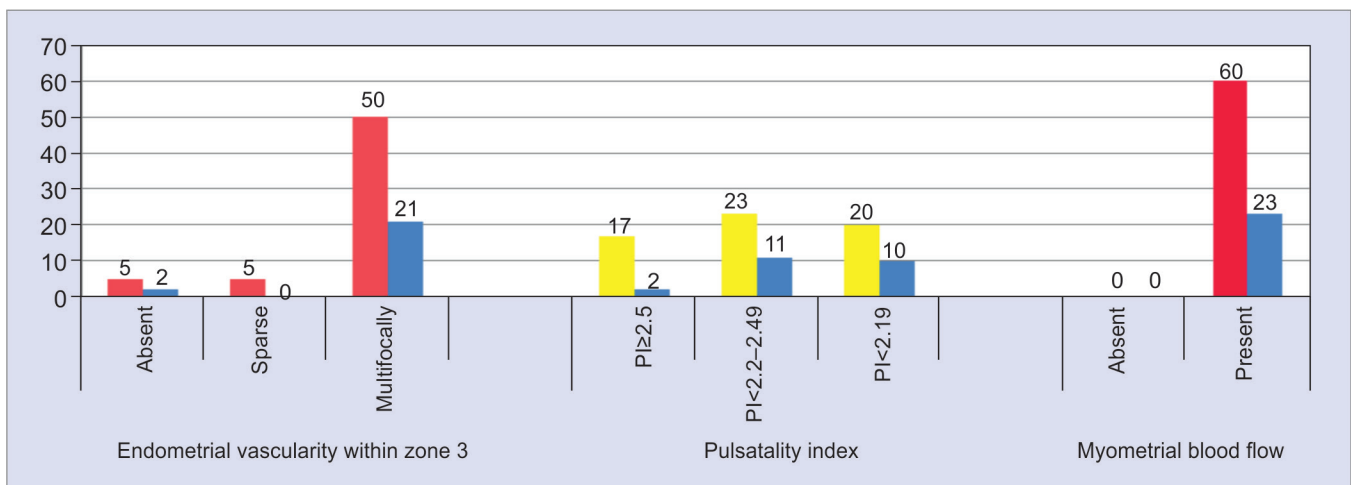


Fig. 2: Correlation of Doppler parameters with pregnancy rate

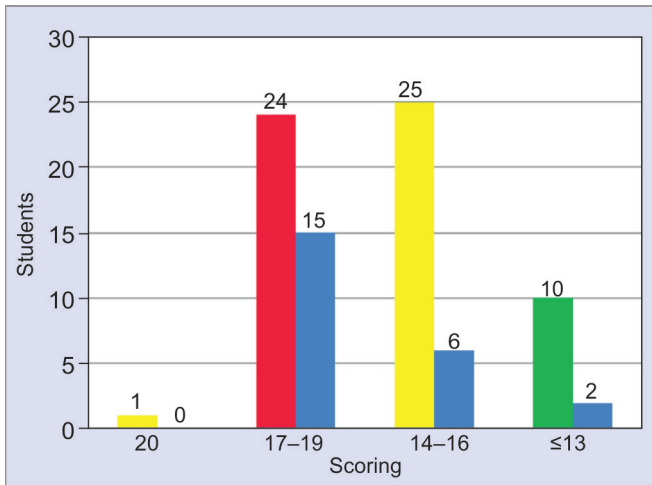


Fig. 3: Correlation of total Applebaum scoring with pregnancy rate

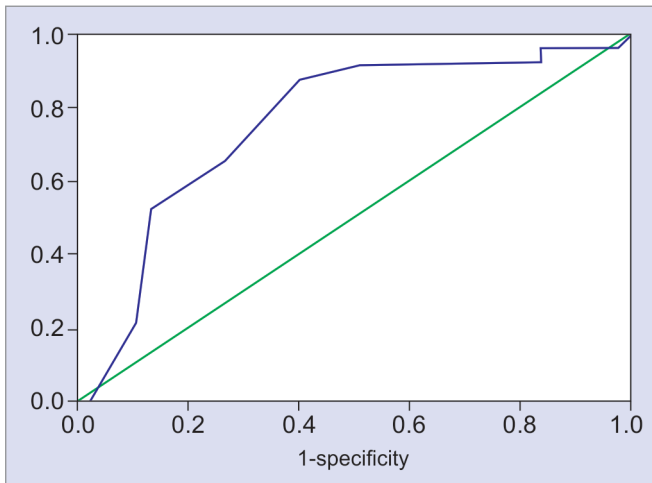


Fig. 4: ROC curve showing sensitivity and specificity of total score in the prediction of pregnancy

## DISCUSSION

Endometrial receptivity has been regarded as a key factor in the success of IVF. Various studies have been conducted to determine the best predictive method for the success of IVF.

In our study, the pregnancy rate decreased with endometrial thickness less than 7 and more than 14. A similar finding was shown by a study done by Kader et al.,<sup>2</sup> which showed that the maximum number of patients i.e. 41% had endometrial thickness between 8 and 10 mm with the pregnancy rate being 50%. The pregnancy rates were 25% and 2.5% in patients with endometrial thickness 10–12 mm and more than 14 mm, respectively. In a study done by Kumari et al.,<sup>3</sup> endometrial thickness between 7 and 14 mm was seen in 91.11% of the patients, out of which 26.67% of females conceived. Shivtare et al.<sup>4</sup> showed that maximum patients i.e. 62% were in the range of 7–9 mm with a pregnancy rate of 47%. Pregnancy rate was maximum i.e. 52% with thickness of 10–14 mm, and no pregnancy occurred with thickness more than 14 mm.

Due to oxygen tension, thinner endometrium results in implantation failure. The high oxygen concentrations near the basal layer could be detrimental compared with the usual low oxygen tension of the surface endometrium. Embryos do not survive at such high oxygen concentration, but no conclusive cutoff value of endometrial thickness has been established.

In our study, women with the distinct five-line appearance of the endometrium showed a higher pregnancy rate compared to that of hazy five-line appearance.

Khan et al.<sup>5</sup> found that 68.5% of women had distinct five-line appearance of the endometrium, out of which 78% conceived; 31.5% of the patients had hazy five-line appearance, out of which 38% conceived. Kumari et al.<sup>3</sup> showed that 58.89% of the patients had distinct five-line appearance, out of which 32% conceived. Shivtare et al.<sup>4</sup> showed that 16% of the patients had distinct five-line appearance of the endometrium, out of which 62% conceived. Biswas and Biswas<sup>6</sup> showed that out of 72% of patients with distinct five-line appearance of the endometrium, 69.4% conceived.

In this study, relatively homogeneous myometrial echogenicity was among the majority of patients i.e. 88.3% with 37.7% of pregnancy rate. Out of the total pregnancy group, 86.9% of the pregnant patients had relatively homogeneous myometrial echogenicity, but it was statistically not significant when compared to the nonpregnant group.

A study done by Khan et al.<sup>5</sup> showed that 92.5% of the patients had relatively homogeneous myometrium with pregnancy rate of 66.48%.

Shivtare et al.<sup>4</sup> showed that 94% of patients had relatively homogeneous myometrium, out of which 75% conceived. Biswas and Biswas<sup>6</sup> showed that out of 38% of patients with relatively homogeneous myometrium, 47% conceived.

Our study showed that the pregnancy rate was higher in patients among whom >3 myometrial contractions were seen in 2 minutes. A study done by Biswas and Biswas<sup>6</sup> showed that 66% of the patients had myometrial contractions >3, out of which 33% conceived. Myometrial contractions (>3 in 2 minutes) toward the fundus improve the implantation rate.

In our study multifocal blood flow (within zone 3) was present among the majority of patients i.e. 88.3%, out of which 42% of patients conceived.

Khan et al.<sup>5</sup> showed that 84% of patients had multifocal blood flow, out of which 76.19% of the patients conceived. Kumari et al.<sup>3</sup> showed that 57.5% of patients had multifocal blood flow (within zone 3), out of which 36.21% of the patients conceived.

For implantation to occur a good blood supply toward the peri-implantation endometrium is an essential requirement.

## CONCLUSION

Uterine scoring was done by TVS, which is a noninvasive, convenient, reproducible, quick, and safe method preferred for endometrial assessment. The uterine scoring system helps us in predicting endometrial receptivity. In our study, uterine artery PI, myometrial contraction, and total Applebaum uterine score parameters were significantly ( $p < 0.05$ ) higher among patients with pregnancy than without pregnancy.

The endometrial receptivity is a predeterminant in predicting the outcome of pregnancy in women. A receptive endometrium is necessary, but not sufficient to ensure implantation. Both

selectivity and receptivity of endometrium are essential for proper implantation.<sup>7</sup> If favorable values of USSR scoring are not obtained, a favorable outcome will not be obtained. Therefore, Applebaum scoring has a higher negative predictive value.

### CLINICAL SIGNIFICANCE

The uterine scoring system helps us in predicting endometrial receptivity.

### REFERENCES

1. Malhotra N, Singh A, Gupta P. Endometrial receptivity and scoring for prediction of implantation and newer markers. *J South Asian Feder Obstet Gynaecol* 2017;9(2):143–154. DOI: 10.5005/jp-journals-10006-1481.
2. Kader MA, Abdelmegeed A, Mahran A, et al. The usefulness of endometrial thickness, morphology and vasculature by 2D Doppler ultrasound in prediction of pregnancy in IVF/ICSI cycles. *Egypt J Radiol Nucl Med* 2016;47(1):341–346. DOI: 10.1016/j.ejrn.2015.08.014.
3. Kumari M, Singh K, Bharti G, et al. Biophysical scoring of the endometrium and intrauterine insemination outcome in the patient with infertility. *Int J Sci Stud* 2017;5(2):120–124. DOI: 10.17354/ijss/2017/230.
4. Shivtare MV, Lad N, Vishwekar P, et al. Uterine scoring system for reproduction scoring correlation with pregnancy rate in infertility patients undergoing intracytoplasmic sperm injection and embryo transfer. *IJRCOG* 2019;8(7). DOI: 10.18203/2320-1770.ijrcog20193057.
5. Khan MS, Shaikh A, Ratnani R. Ultrasonography and Doppler study to predict uterine receptivity in infertile patients undergoing embryo transfer. *J Obstet Gynaecol India* 2016;66(Suppl. 1):377–382. DOI: 10.1007/s13224-015-0742-5.
6. Biswas S, Biswas S. Transvaginal sonography in unexplained infertility: a study. *J Gynecol* 2017;2(3):000147.
7. Sahoo G, Agrawal V. How to improve thin endometrium in cases of female infertility. *J South Asian Feder Obstet Gynaecol* 2018;10(2):81–83. DOI: 10.5005/jp-journals-10006-1565.